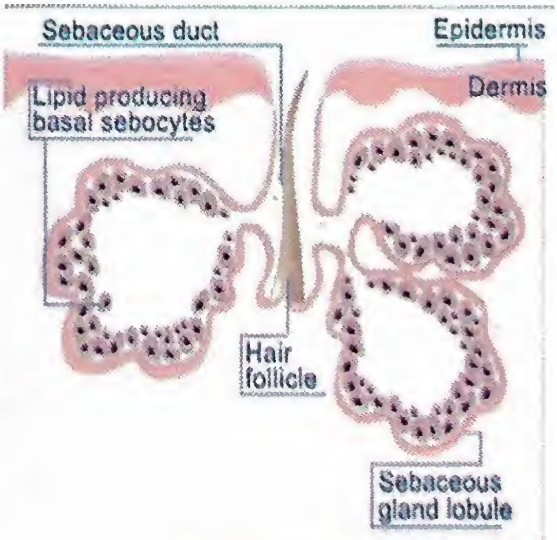
9 Diseases of Sebaceous & Sweat Glands

Sebaceous Glands

Structure and physiology

- **Sebaceous glands are holocrine glands,** i.e. their secretion is formed by complete destruction of the cells. The transit time of cells from formation to discharge is 7.4 days in average.
- Each sebaceous gland consists of many lobes, each with a duct lined by stratified squamous epithelium. All ducts converge toward the main sebaceous duct which opens into the pilosebaceous canal whose epithelium is continuous with surface epidermis.
- **They are distributed all over skin surface** except palms & soles. They are large and numerous in midline of back, forehead, and face (about 400-900 glands/cm^2 while elsewhere >100/cm^2).

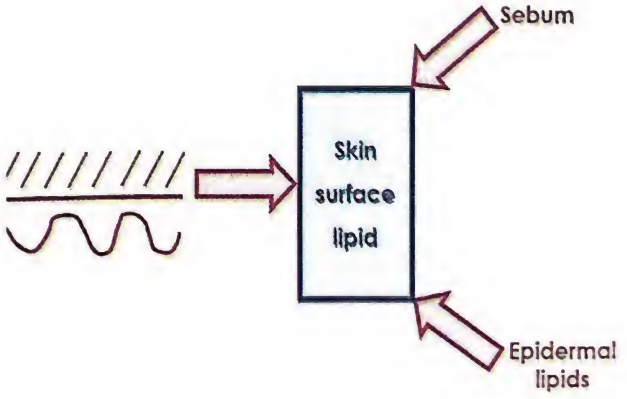


Sebaceous follicle

- **Free sebaceous glands** (not associated with hair follicles) open directly to surface of the skin, e.g. Meibomian glands of eyelids, Tyson's glands of prepuce, in female genitalia, and in the areola (Montgomery glands).
- Sebaceous glands develop in the 13th to 15th week of intrauterine life (IUL) originating as budding cells from the primordial follicular epithelium (buds from developing hair follicle root sheaths).
- Sebum is the 1st glandular product of human body. In IUL, they are regulated by maternal androgens. They remain active in neonatal period, but then involute in early childhood till puberty, where they undergo enlargement → ↑ sebum excretion.

Composition

- Sebum is a complex mixture of lipids. However, surface skin lipid film contains not only sebum but also lipids from keratinizing epidermis.
- Skin surface lipid consists of triglycerides (TG), free fatty acids (FFAs), cholesterol & cholesterol esters, wax esters & squalene (the last 2 are produced only by sebaceous glands).



- FFAs are formed in sebaceous ducts by effect of lipolytic enzymes on TG.

Sebum composition

	Isolated gland (%)	Epidermal lipids (%)	Skin surface* (%)
TG	57	65	42
FFAs	0	0	15
Wax esters	25	0	25
Squalene	15	0	15
Cholesterol esters	2	15	2
Cholesterol	1	20	1

**After hydrolysis of TG by bacteria*

> The sebaceous glands do not convert squalene to sterols, whereas in epidermis, squalene synthesized in the lower layers is rapidly & totally converted to sterols, either to precursors of Vitamin D or to cholesterol. **Squalene is unique to sebum & is virtually unique to humans.**

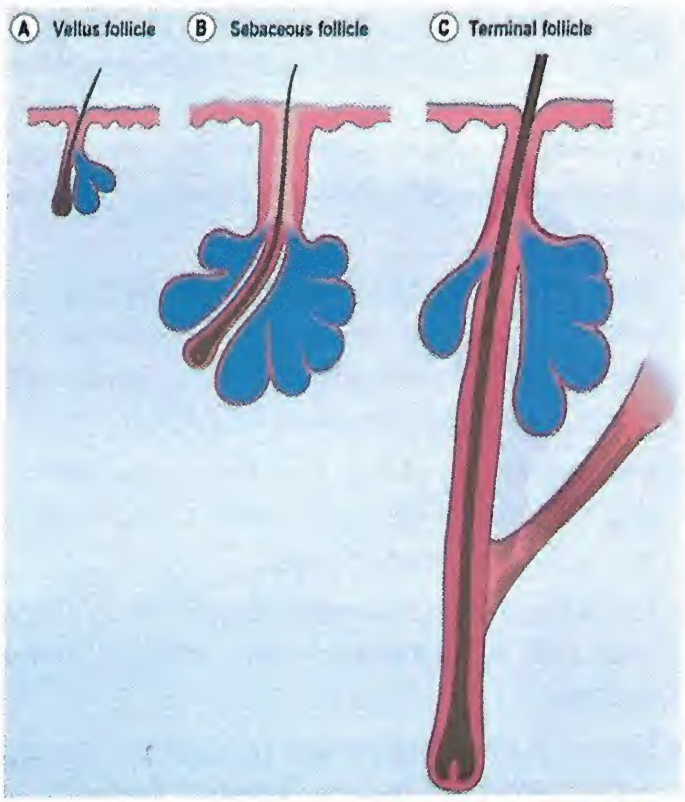
1

Types of pilosebaceous follicles

A) Terminal follicles: Characterized by long coarse terminal hairs & are situated in adults on scalp, beard, eyebrows, axillae & pubes. Acne does not develop in these follicles as the powerful erecting hair allows free excretion of sebum.

B) Sebaceous follicles: Where acne develops. They are characterized by large sebaceous gland & rudimentary hair follicles producing fine hairs which cannot withstand sebum production. They are present mainly on face, shoulders, upper back & sternal region (sites of acne predilection).

C) Vellus follicles: With fine, soft hairs covering most of body of youngsters. With the onset of puberty, prepubertal vellus hairs in the beard, scalp, pubic & axillary regions become terminal hairs, while in the sites of predilection, become sebaceous follicles.



Bolognia et al., Dermatology Textbook, third edition, 2012.

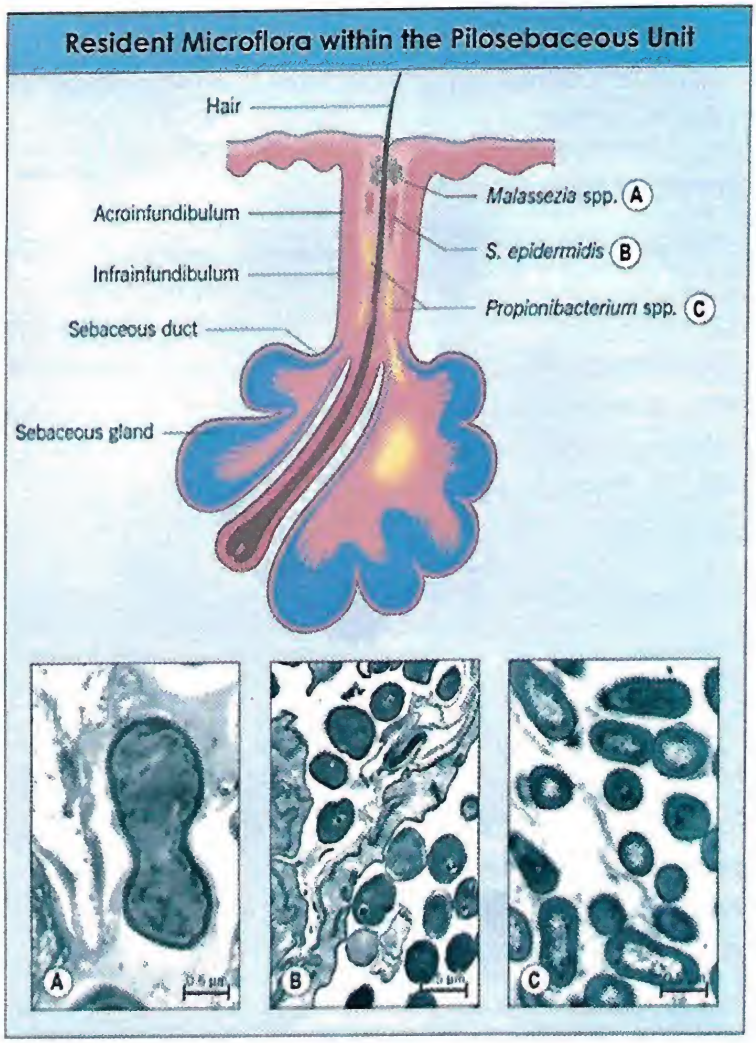
Resident microflora within the pilosebaceous unit

A Malassezia.

B Staphylococcus epidermidis.

C Propionibacterium spp.: There are three species of propionibacteria: P. acnes, P. granulosum and, the least common, P. parvum.

Pilosebaceous units also harbor Demodex mites, which increase in number in older adults and are rarely seen in prepubertal children.



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Functions of sebaceous glands/sebum or lipid film

1. Control moisture loss from epidermis.
2. Protection against fungal & bacterial infections:
   - Certain surface FFAs markedly reduce the growth of pathogenic organisms, such as Staphylococcus aureus, and suppression of sebaceous gland activity by isotretinoin may be followed by impetigo towards the end of a 4-month course.
   - Sebum or at least the product of its hydrolysis, is fungistatic. Fungi causing tinea pedis preferentially colonize areas that are not supplied with sebaceous glands and ringworm of the scalp becomes rare after puberty, when sebum production increases.
3. Thermoregulatory role: Under hot conditions, their secretions emulsify eccrine sweat, leading to the formation of a sweat sheet which helps prevent the loss of individual sweat drops from the skin. In colder conditions, sebum changes its nature and repels rain from skin and hair.
4. Sebocytes are capable of metabolizing and synthesizing the primary vitamin D metabolite 1,25-dihydroxyvitamin D3.
5. The sebaceous gland also secretes vitamin E (antioxidant) into the upper layers of the facial skin. This may serve to protect skin surface lipid and the upper stratum corneum from harmful oxidation.

Measurement of sebaceous activity

By placing a pad of cigarette papers for 3 hours on a limited area of forehead & then the sebum is extracted with diethyl ether.

Control of sebaceous glands activity

1. **Androgen:** Sebaceous gland is an androgen target organ. Administration of testosterone increases the size of the glands & sebum output of prepubertal boys, but not of adult males, where the glands appear to be under maximal stimulation of endogenous androgen. Sebaceous gland activity varies from follicle to follicle & this may reflect different sensitivities to the effects of androgens, possibly due to variability in androgen receptor content or varying local levels of 5α-reductase, an enzyme which converts testosterone into the more active form dihydrotestosterone (DHT). The conversion of testosterone to DHT is 30 times higher in acne skin than in normal skin.
2. **Progesterone:** It has no clear effect except in very large doses → stimulation of sebaceous glands.
3. **Estrogen:** It depresses sebaceous activity by reducing endogenous androgen production or it may act at peripheral site directly on sebaceous glands.
4. **Glucocorticoids:** They inhibit sebaceous gland activity through either suppressing adrenal androgen production or by direct effect.
5. **Pituitary hormones:** They increase sebaceous gland activity either by direct effect (α-melanocyte stimulating hormone), or indirectly through release of gonadal, adrenal or thyroid hormones. A sebotropic hormone may be present.
6. **Corticotrophin releasing hormone (CRH) and CRH-receptor-1:** Increased levels are present in sebaceous glands of patients with acne vulgaris. They increase lipid and androgen synthesis and increase production of IL-6 and IL-8.

Other factors controlling sebaceous glands activity*

7. **Retinoids:** Histological changes in sebaceous gland size can be seen after 8 weeks of treatment. The sebaceous glands became smaller in size and the sebocytes appear undifferentiated with decreased lipid accumulation.
8. **Peroxisome proliferator-activated receptors (PPARs):**
   - They are nuclear receptors that mediate epidermal growth, differentiation, & lipid metabolism.
   - There are three subtypes of PPARs (α, β, and γ1 – γ3) that differ in their tissue distribution and respective roles in mediating lipid metabolism.
   - PPARα ligands increase the formation of cornified envelopes, the expression of differentiation proteins and increases the mRNA for a variety of lipogenic enzymes.
9. **Insulin-like growth factors (IGF):**
   - There are two forms of IGF: IGF-1 and IGF-2, with IGF-1 being the most abundant.
   - IGF-1 interacts with receptors on the sebaceous gland to stimulate its growth.
   - The actions of IGF-1 on sebaceous glands can be mediated by androgens.
   - Insulin can also act at the IGF-1 receptor, although with a 2-fold decreased affinity.
10. **Epidermal growth factor and keratinocyte growth factor** can stimulate the growth of sebaceous glands.

** Journal of Lipid Research, Volume 49, 2008.*

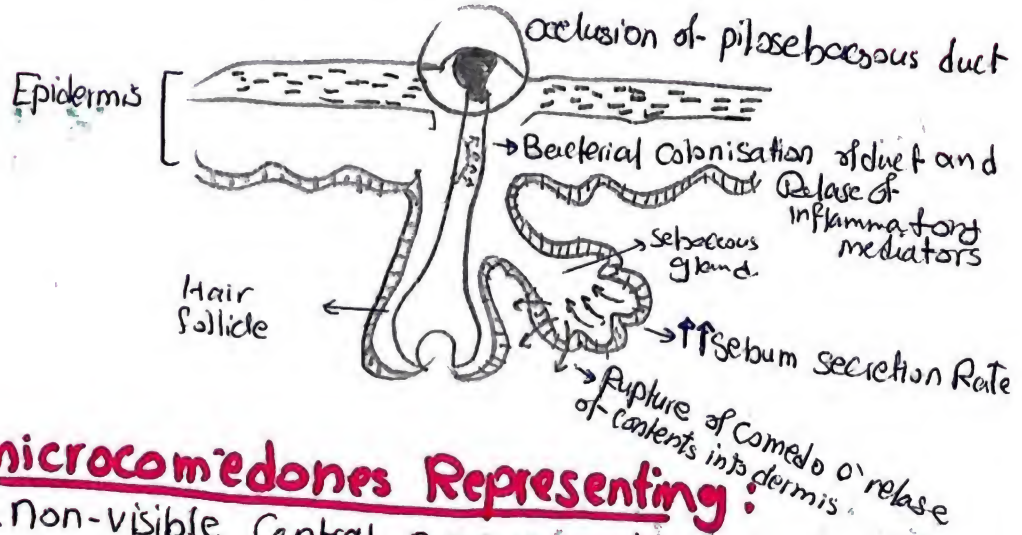
Acne Vulgaris

- **D.f**: chronic inflammatory Disorder of pilosebaceous apparatus.
  - ch.chBy: Formation of Comedones, nodules → papules, Cysts → pustules
  - its a chronic Disease.

- **Epidemiology**:
  - start in adolescence, Both sexes
  - Resolve By: mid-twenties
  - Boys: have peak incidence 16-19 yr
    girls: 14-16 yr.

- **Etiopathogenesis**:
  - Initial → microcomedo → **microcomedones Representing**:
    - non-visible central precursor lesions of acne. are induced By sebaceous Hyperplasia. aswell as altered follicular growth and differentiation.
    - evolve into Both Comedones and inflammatory lesions.
  - True Acne: follicular eruption of Comedo → initiates inflammatory Reaction → papules, pustules, Cysts
  - Disorders as: rosacea. steroid acne → Similar to acne [acneform eruption].

- **ch.ch of acne → define chronic disease**:
  1. pattern of Recurrence or Relapse.
  2. prolong course.
  3. acute outbreaks - slow onset
  4. Psychological - Social impact



•AV is multifactorial disease involving 4 main pathologic events:

① ↑ Sebum production:

1. acne ptn secrete more sebum
2. The level of secretion Correlates with The severity of acne.
3. occur Due to: androgenic stimulation at The time of puberty →
   Cute: End-organ hyper-Response of the gland to normal level of plasma androgens
4. This is Supported By: the clinical observation That many ptns only Have acne at Some But Not All Sebaceous sites
5. No ↑↑ in androgen levels in most acne ptn.

② Ductal Hyper Cornification: "Comedone"

1- its Due to: excessive accumulation of Ductal Corneocytes D.t ↑↑ formation or inadequate separation of Ductal Corneocytes.

2- Ductal Cornification Result from: - androgen Stimulation, and the irritant effect of sebum: -
- → Squalene
- → Squalene Oxide
- → PPARs
- → IL-1 → produced By lymphocytes and Keratinocytes.

3- Deficency in sebum
- → essential FFA
- → lindeic Acid → Demonstrated in Comedones.

4- this deficency is Reversed: -
During Isotretinoin OR Cyproterone acetate ↓↓.

③ Proliferation of propionibacterium acne "P. acne": (facultative anaerobes)

1- in the anaerobic micro environment → Created By: the Blocked sebaceous follicle.

2- P. acne → Secrete Lipases → which cleave lipids in sebum into pro-inflammatory FFAs.
Both: Comedogenic and chemotactic

3- P. acnes → Bind/activate toll-like receptor 2 (TLR2)

④ inflammation:

1- the inflammation in acne lesions is Duets: the liberation of lipase enzyme from p. acnes → that produce FFAs from TG → leading to: erosions + disruption of follicular wall. with escape of follicular contents to the Dermis with → production of non-specific inflammatory Reaction.

2- it was found that → Ductal Rupture is Not necessary for the initiation of inflammation. as: upto 80% of early inflammed acne lesions arise without Rupture of the Duct.

→ 2 stages of inflammation:

A) Early inflammation

→ inflammatory events found to precede: Hyperkeratinization
↳ CD_4 cells number and IL-1 activity → ↑↑ prior to Hyperkeratinization.

Androgen stimulation + Sebum imitation → Ductal Cornification → plugging of the follicle (Comedone) → Anaerobic micro environment → Proliferation of P. acne

- androgen Receptors: present on Basal layer of sebaceus gland and outer Root of sheath of Hair follicle
  - respond to most potent androgen DHT Testosterone
- TLRs → family of Transmembrane protiens → Directly implicated in the recognition of microbial pathogens including: peptidoglycan components of The Coats of P. acnes.

B) severe - nonspecific inflammation:

- Result from → Rupture of the follicle + - liberation of the follicular contents into the dermis

• Toll-like Receptor TLR:

1- p.acne → Cause inflammation By:
Activation of TLR2 on the suiface of perifollicular inflammatory cells

2- proinflammatory Cytokines ← IL-1B, IL-8, TNF-α
Relased By:- perifollicular inflammatory cells
upon activation By P.acnes

3- IL-8 → Result in → Neutrophil Recruitment
→ Relase of lysosomal enzymes
→ Disruption of follicular epithelium

4- TLR2 → Expressed in: Basal and infundibular Keratinocytes, sebaceous glands
its activation → provokes the Release of IL-1α from Keratinocytes.

5- TLR2 → activation and secretion of IL-1α from Keratinocytes → initiating steps in Comedogenesis

• B-defensins:

1- pro-inflammatory Cytokines ← Interleukin-1B, TNF-α
+ Bacterial Lipopolysaccharides → upregulate B-defensins.

2- Upregulation of B-defensins expression in AV lesions → suggest that B-defensins may involved in the pathogenesis of AV

3- antimicrobial peptides (AMPs) → That are part of the innate immune response.

4- made; endogenously By → Keratinocytes, sebocytes.

• Inflammatory Cytokines:

1- working via autocrine and paracrine mechanism.

2- through their respective Receptors → amplify the signaling pathways that activate the activator proteins (AP)-1 transcription factor.

- Activation of AP-1 induces matrix metalloproteinases (MMP) gene
- whose products degrade and alter the dermal matrix

- MMPs occur in sebum and ↓↓ eHH-related resolution of acne lesions

• Pathophysiology:

1- inflammatory events → precede Hyperkeratinization
2- P.acnes → Contributes to inflammation via activation of TLR on the membrane of inflammatory cells
3- Peroxisome proliferator-activated receptors partly → Regulate → Sebum production
4- The Sebaceous gland is → neuro-endocrine inflammatory organ → executes a Local Response to stress and normal functions.
5- Androgens → have influence on follicular Corneocytes
6- Oxidized Lipids → in sebum Can stimulate production of inflammatory mediators
7- Matrix metalloproteinases (MMPs) occur in Sebum + ↓↓ e` ttt-related Resolution of acne lesions
8- The inflammation is Not an abnormal Response of the immune system, But it Represents a normal immune System But → it represents: a normal immune and non-immune response to foreign substances

• Role of estrogens in acne pathogenesis :-

1- Directly opposing The effect of Androgens Locally within the sebaceous gland
2- inhibiting the production of Androgens By: gonadal tissue via: -ve feedback Loop whereby pituitary gonadotropin relase is inhibited
3- Regulating genes that -vely influence Sebaceous gland growth or lipid production

• Other factors in the etiopathogenesis of AV :-

① Genetic :- → family History +ve
② Diet :- 1- High glycemic diets → exacebate acne
2- milk → influence Comedogensis D.t:
- Contain androgens - 5α reduced steroids
- Contain insulin-like growth factor 1 (IGF-1) produce Hyper insulinemic response

↳ The hormones in milk are Carried By:-
The whey protien fractions → Contain insulin secretagogues.
↳ elevated insulin & IGF-1 levels 2ry To Dietary influences Can increase Testosterone production

③ **Premenstrual flare**: 70% of ♀

④ **UVR**: → improve acne OR → enhance the Comedogenicity of Sebum

⑤ **Stress**: exacerbate acne

⑥ **Occupation**:
- Hydration of st. Corneum → may induce acne: → steam cleaning
- ptn Dealing ē oil → oiLacne (Trunk limbs)

⑦ **Sweating**: 15% of acne ptns → sweating Causes deterioration of their acne.. Specially: who live or work in hot humid environment e.g: Cook.
- Ductal hydration may be the responsible factor.

• Acne resolution :-

- in most Cases → Acne Resolve in Early adult life.
- But the reason for resolution is Not clear
- it does not appear to be related to a reduction in Sebum production or Suiface Bacteria.
- it may be related to:- Change in Response in the follicle to Androgen → which No Longer produces inflammation

• Clinical picture :-

- **Site**: Face - Chest - Shoulders - upper Back
- **the lesion**: polymorphic
- **the pathognomic lesion**: non-inflamed lesion (Comedone)
- **Types of Comedones**:-

1. open Comedones: (Blackheads)
   Black color maybe Due to the presence of melanin or oxidized sebum
2. Closed comedones: (whiteheads)
3. intermediate Comedones: (Both Black-white heads)

4 Sandpaper Comedones:
- Multiple . very small whiteheads.
- most often in forehead
- many as 500 lesions → Rough to touch

5 Macrocomedones:
- Large whiteheads > 1mm in diameter

6 Submarine Comedones:
- Large comedonal structures > 0.5 cm, occur deep in skin

7 2ry Comedones:
- Include → Chloracne
  → Pomade acne
  → Steroid acne

* as the Disease progresses → Inflammatory lesions as → papules
  Cysts ↔ pustules
  nodules

* its unusual for Blackheads to Develop into inflamed lesions
- But 70% of whiteheads Develop into inflamed lesions

* Seborrhea → universal feature → Related to severity of the Disease.

* as Acne Resolve → post inflammatory Erythema + even pigmentation may occur.

* The Deeper inflammatory lesions → Scar

• Scar •

* ↑↑ tissue formation
  1. Keloid
  2. Hypertrophic scar

Tissue Damage
- Atrophic scar

Ice pick :-
< 2mm (smaller in Diameter)
Deep è tracts to the dermis or subcutaneous tissue

Boxcar
> 1-4mm
(< 0.5mm)
- Shallow
- OR Deep (> 0.5mm)

Rolling : soft
- Circular or linear. > 4mm
- have gently sloped edges → that merge è normal appearing skin

★ Scars are more likely to occur in ptns:

- → Genetically prone to scarring
- → Acne for Long time, even è moderate Types
  - è Sever Deep inflammatory Acne
  - è Severe exacerbation (flare-up) è Isotretinoin therapy

★ Early, nonspecific inflammation → Result in Less scarring than of Delayed specific inflammatory Response

★ Mechanism of Scarring:

- Its an consequence of → Abnormal Resolution or wound healing following The Damage that occur in Sebaceous follicle During acne inflammation.
- in ptn prone to scarring → There is chronic Delayed Type-1 Hyper-Sensitivity Reaction → provoked By a resistant antigen
  - which These ptns unable to eliminate.

★ Early, appropriate treatment is the Best to minimize the potential of acne Scar:

- → Scarring → is the 1ry Concern of ptn è Acne.
- → the ttt of scar → according to: Scar ch.ch.
  - Involve:
    - resurfacing
    - Surgical revision
    - Dermal Fillers
    - Topical Retinoids
- → 2 Key modifiable factors linked to Scars:
  - time Delay Between onset of Acne and effective ttt.
  - the extent / Duration of inflammation
- → Early appropriate ttt → that Continued for as Long as necessary → is the Best way to prevent Scarring
- → The progression of Scarring → Despite Aggressive Traditional ttt → is a 1ry rationale for use of Oral Isotretinoin

III D.t Ectopic hormone production:

- Ectopic ACTH secretion By:
  - lung Carcinomas
  - Carcinoids
- production of- B-HCG By:
  Choriocarcinoma.

IV Iatrogenic hirsutism:

- Due to: Anabolic steroids Adminstrate to women
- once steroid Discontinued → Hirsutism improves

V] Hepatic Hirsutism:

- with Liver Disease: ↓↓ in Sex Hormone-Binding globulin (SHGB).
- more free testosterone → Conversion to DHT

VI D.t peripheral Faliure in Converting Androgen in to Estrogen: ↑↑↑ free testosterone.

*HAIR-AN syndrome:

HyperAndrogenism. Insulin Resistance, Acanthosis Nigricans

4* DD:

Defeminization	Virilization
- Acne	- Hirsutism
- Female androgenic Alopecia (FAGA)	- Female androgenic Alopecia of male pattern (FAGAM)
- Menstrual alteration (Oligo)	- Amenorrhea
- Breast atrophy	- Muscle mass ↑↑
- Loss female Body contours	- Clitromegaly
- Rugosity of vaginal column ↓↓	- Coarsening of Voice
- Infertility	

5-Evaluation of ptn: 1-Histry 2-examinfion 3-Lab invest

① History:- • Age of onset • rate of progression • medication • virilization Symptoms • menstrual • family • pregnancy

→ if History of: Rapid progression, Sudden onset of Hirsutism and Virilization → Neoplastic Source.

- treatment:

1- Bed Rest, hospitalization
2- Surgical debridement, warm Compresses of 20-40% Urea Solution.
3- Topical ttt e` antibacterial cleansers.
   - medicated Lotions
   - Topical High potency Corticosteroid.
4- Systemic ttt: Isotretinoin alone OR Combined e` Systemic Corticosteroids
   - Non Steroidal anti-inflammatory Drugs For → Myalgias

③ Acne Conglobata and associated conditions:

* primary defect: Alteration of Keratinization within the Sebaceous Follicle and leakage of Retained sweat → into tissue. Surrounding plugged ecrine ducts
* mainly in: Young males
* Site: Trunk, face, limbs
* many pts Dont have preceding AV lesions
* Ch.ch By: Nodules, tender Large cysts may fuse to form: multiple Draining Sinuses
* Grouped multiple fused Blackheads and Scarring of the Keloidal type.
* Acne Conglobata Differentiated from Acne vulgaris By:
  - occurrence late in life
  - its Unremitting Course
* Hidradenitis Suppurativa:
  - may be found in some patients
* - its a Part of follicular occlusion Triad
* treatment:
  Usually Dont Require Oral Steroids
  Start Oral Isotretinoin immediatly

④ Gram -ve folliculitis:

→ its a Complication of: prolonged ttt of AV e` Broad Spectrum Antibiotics.
→ ch.ch By: Superficial pustules grouped around the anterior nares or nodular cystic lesions.
→ Culture: E.coli . Klebsiella . proteus pseudomonus

→ Treatment:

- Current antibiotic → Discontinued
- good Gram-ve antibiotic ↑↑ used.
  ↳ e.g: Oral trimethoprim (200-300 mg /twice/ daily)
- ↳ Isotretinoin for Resistant Cases.

Differentiation between acne fulminans & acne conglobata

	Acne fulminans	Acne conglobata
Sex	Men	Men>women
Age	13-16 years	20-25 years
Onset	Sudden	Slow
Localization	Face, neck, chest & back	
Clinical features	Hemorrhagic ulcerations	Nodules, cysts, polyporous comedones
Systemic signs & symptoms	Very common; malaise, fever, leukocytosis, elevated ESR, polyarthralgia, osteolytic bone changes, proteinuria, erythema nodosum, hepatomegaly, splenomegaly	Uncommon
Response to systemic antibiotic therapy	No	Yes

⑤ Acne excoriee des Jeunes filles:

- AV è excoriation of lesions
- Seen in: girls who have → superficial mild acne.
- The primary acne lesions are small or even non existent
- But: the ptn have compulsive habit of picking and squeezing them.
- its a subset of neurotic excoriations
- often associated è Obsessive Compulsive disorder
- Use of: Doxepin - SSRI → may be beneficial

⑥ Solid facial edema (Morbihan's)

- Unusual and disfiguring Complication of Acne vulgaris
- Clinically: Distortion of the middleline face and cheeks
- Due to: Soft tissue Swelling
- The woody non-scaling induration may be accompanied By: Erythema
- No spontenous Resolution.
- Treatment: Isotretinoin alone or è Ketotifen or prednisone (10-30mg/day) For 4-5 months

⑦ Acne Mechanica:

- Occur: at site of physical Trauma.
- e.g: head Bands in sports men and hippies
- tight brassiere straps and on The neck of vipllin players

⑧ Drug-induced acne:

(Acne medicamentosa)

- Some Drugs may aggravate AV. or induce acneiform eruptions

Drugs reported to cause acne or acne-like eruptions (Acne medicamentosa)

Hormones & steroids • Gonadotrophins. • Androgens. • Anabolic steroids. • Oral & topical steroids. **Halogens** • Bromides. • Iodides. • Halothane. **Anti-epileptic drugs** • Diphenylhydantoin (phenytoin). • Phenobarbitone. • Troxidone.	**Anti-tuberculous drugs** • Isoniazid. • Rifampicin. **Miscellaneous** • Chloral hydrate. • Cyanocobalamin. • Disulfiram. • Lithium. • Psoralens (with UVA). • Quinine. • Sulphur. • Thiouracil. • Thiourea.

- Drug: Steroid acne:

- Steroid induced keratinization in the upper pait of the pilosebaceous Duct.
- it is Ch.ch By:- sudden apperance of inflamed papules and pustules, è sparse or absent Comedones.
- mainly in: upper trunk, arm, rarely face.
- The lesion is monomorphic than AV - ↓↓ and stopage of Drugs.

- post inflammatory Hyperpigmentation Common
- treatment: Tretinoin 0.05% + stop Drug.

⑨ ACne D.t external chemicals:

(Acne venenata)

- These chemicals induce Acne through follicular Hyperkeratosis

⊛ Acne Cosmetica:

-makeups containing Lanolin, petrolatum oleic acids are Comedogenic

⊛ pomade acne:

- in Blacks D.t :- application of various greases oils to scalp Hair and Face as grooming aid.

⊛ Occupational acne:

D.t oils, tars e.g: Lubricating oils

⊛ Chloracne:

D.t: exposure to the chlorinated Hydrocarbons e.g: Chloro-di-phenyloxide -Polyhalogenated e.g: Dioxin

⊛ Crude Coal tar

⊛ Acne Detergicans:

with over-wash with soaps that contain Hexachlorophene

(10) Neonatal Acne:

[neonatal Cephalic pustulosis]

- Neonatal acne 20% of newborns
- present at Birth or Develop During First few months of life
- more common in males
- mild - regresses spontaneously in most cases By ages
- pathogenesis:
  - ↳ several Malassezia (furfur, sympodialis) proposed as the etiology
  - ↳ as a clinical response to treatment with topical 2% Ketoconazole Cream.
  - ↳ After Birth: neonatal sebum excretion rates → tend to match the high levels seen in mothers

(11) Infantile acne:

- begins Between the 3rd, 6th month of life
- may persist to age of 5
- it's rare, more common in males
- it Can be severe ← nodules, cysts
- significant residual scarring
- Some cases associated ← Tumors
- pathogenesis:
  - ↳ hormonal imbalances intrinsic to this stage of Development (↑LH, testosterone, DHEA)

Comparison of trends in acne for various ages

Age group	Location	Morphologic condition	Sex
Neonates	Nose, cheeks, forehead	Comedonal	Both
Infants	Face	Inflammatory	Males
Preteens (Figs 19, 20)	Centrofacial	Comedonal	Both
Teens	Face, trunk	Mixed	Both
Adults	Perioral, jawline, chin	Inflammatory	Women

(12) Endocrinologic abnormalities:

- most ptn ← Acne, Don't have over endocrinologic abnormalities
- it's a sign of Hyperandrogenism
- Check Hormonal levels [LH, FSH, DHEA-S]

(13) Apert syndrome:

- Result from: mutations in FGFR2 → which encodes fibroblasts growth factor receptor 2
- mutation in FGFR2 observed in Nevus Comedonicus

- Skin manifestations:
- Acneiform papules < Diffuse involve the entire extensor of the arms Buttocks, thigh.
  - Highly Resistant to topical therapies
  - Respond to Isotretinoin
- marked Seborrhea
- Nail Dystrophy
- Cutaneous + ocular Hypopigmention

(14) Vasculitic/pyoderma gangrenosum Acne:

- Clinically :-
  - Few pts who have mild acne → develop Sudden onset of severe vasculitic, Pyoderma gangrenosum-like lesions
  - it heals è significant scarring
  - The mechanism is: Immunological Reaction to P. acnes.
- treatment:
  - UnResponsive to oral Isotretinoin alone
  - Respond to oral steroids and Azathioprine (200mg 1day) over 3-4 months periods

Syndromes associated with acne*

Syndrome	Clinical features
PAPA syndrome	Pyogenic **A**rthritis (sterile), Pyoderma gangrenosum, **A**cne • Inherited (AD), CD2 binding protein 1 (CD2BP1) mutation; CD2BP1 is a pyrin-interacting protein, which is part of inflammatory pathway associated with familial Mediterranean fever, Muckle-Wells syndrome, & familial cold urticaria. • Skin changes typically present near or at puberty.
HAIR-AN	**H**yper**A**ndrogenism, **I**nsulin **R**esistance, **A**canthosis **N**igricans.
SAPHO (Chronic recurrent multifocal osteomyelitis)	**S**ynovitis, **A**cne (conglobata), **P**ustulosis (palmoplantar), **H**yperostosis, **O**steitis • Inflammatory bone changes (commonly involving sternoclavicular joint, spine "spondyloarthropathy" & long bones); peripheral arthritis also common • 1st line treatment: Bisphosphonates suggested in many case reports & series; other treatments include mainstay therapies for psoriatic arthritis (methotrexate, anti-TNF-α agents, ... etc).

*Adapted from: Jain, Dermatology Illustrated Study Guide and Comprehensive Board Review, 2012.

• Histopathology of AV:

Comedo
- Keratinous debris
- micro-organisms
- fragments of Hair & sebum
- Two Types

closed white
melanocytes normally present in upper part of infundibulum & few melanin

Black Comedo
numerous
Large
enzymatically active melanocytes
melanin in outer portion

- After Rupture of follicular wall and escape of its contents into dermis
  - ↓ if There is Small aggregation of neutrophils → Pustules
  - if the aggregation is Large - deep → Nodules

Papules
- lymphocytic perifollicular infiltrate

• treatment:

★ Factors associated è Better adherence with acne therapy:

① ptn demographic factors:
- older age - Being married - female

② Medication ch.ch:
- Oral Isotretinoin Vs other regimens
- Gel Formulations Vs other topical antiacnes. formulation
- once daily formulation
- Convenient formulation e.g: No need to refrigate

③ patient preferences: - satisfaction è ttt
- pleased è physician

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Drugs used in the treatment of acne:

(I) Topical	(II) Oral	(III) Miscellaneous
Predominantly anticomedonal	***Antibiotics***	• UVR.
• Topical retinoids	***Hormonal regimens***	• Liquid nitrogen.
• Adapalene.	***Antiandrogens***	• Intralesional steroids.
• Azelaic acid.	***Retinoids "isotretinoin"***	• Lasers.
Predominantly antimicrobial	***Other oral therapies***	• Microneedling and platelet rich plasma (PRP) for atrophic acne scars.
• Topical antibiotics.		
○ Erythromycin.		
○ Clindamycin.		
○ Tetracycline.		
○ Erythromycin + Zinc.		
• Azelaic acid.		
• Benzoyl peroxide (BP).		
• Benzamycin (Bp + erythromycin).		
Predominantly anti-inflammatory		
• Adapalene.		
• Topical antibiotics.		

* Assessment of acne severity:

- Done before Rx
- Includes:
  - Type of lesion: Comedonal / inflammatory / mixed.
  - Psychological
  - Presence of Scarring

① mild acne:

→ Require topical therapy only

Non-inflammatory predominantly

- Retinoic acid 0.05%
- Azelaic acid 20%
- Adapalene
- Comedone extractor
- α. Hydroxy acids esters (AHA)

Inflammatory predominantly

- Benzoyl peroxide
- Topical Antibiotics
  - Clindamycin
  - erythromycin
  - Erythro + Zn acetate
- Azelaic acid 20%
- Adapalene
- Zinc gluconate

Mixed

- BPO (Benzoyl peroxide) + Erythromycin (Benzamycin)
- Retinoids (T) + Antibiotics (T

② Moderate to severe

- Systemic Therapy as
  - Oral antibiotics
  - Cyproterone acetate

in conjunction ∈ appropriate Topically Therapy

③ Severe acne:

= Isotretinoin

(young males ∈ marked seborrhea + truncal acne
Respond less well than females ∈ facial acne)

* ~~Topical~~

* The fact that Microcomedones are subclinical and Not apparent to the naked eye → underscores the need to apply Topical therapies to the entire affected area.

Treatment of acne vulgaris

Treatment of acne vulgaris					
	Mild		Moderate		Severe
	Comedonal	Papular / pustular	Papular / pustular	Nodular	Conglobata / fulminans
First line	TR	TR + topical antimicrobial*	Oral AB† + TR ± BPO		Oral Iso (may require concurrent oral corticosteroid, esp. for acne fulminans)
Second line	Alternative TR AA Salicylic acid	Alternative TR + alt. topical anti-microbial AA Salicylic acid Topical dapsone	Alternative oral AB‡ + alt. TR ± BPO/AA	Oral Iso Alternative oral AB† + alt. TR ± BPO/AA	Dapsone High-dose oral AB + TR + BPO
Options for female patients			Oral contraceptive / antiandrogen		
Surgical options	Comedo extraction		Comedo extraction	Comedo extraction ILCS	ILCS
Refractory to treatment		Exclude gram-negative folliculitis			
			• Female patient: Exclude adrenal or ovarian dysfunction. • Exclude use of anabolic steroid or other acne-exacerbating medications.		
Mainte-nance			TR ± BPO		

* *Antibiotic (e.g. clindamycin, erythromycin or sodium sulfacetamide) &/or BPO.*

† *Tetracycline derivatives.* ‡ *e.g. azithromycin or trimethoprim-sulfamethoxazole.*

TR: Topical retinoid, Oral AB: Oral antibiotic, Oral Iso: Oral Isotretinoin, AA: Azelaic acid, ILCS: Intralesional corticosteroid

Bolognia et al., Dermatology, third edition, 2012.

Suppression	Sebum	Comedones	P. acnes	Inflammation
• **Bpo (T)**	-	±	++	+
• **Antibiotics (T)**	-	-	++	+
• **Retinoids (T)**	-	++	-	? ±
• **Sebium AKN (T)**	? ±	+	+	+
• **Azelaic acid (T)**	-	+	++	+
• **Tetracycline (S)**	-	-	++	+
• **Isotretinoin (S)**	+++	++	+	++

(S) = Systemic, (T) = Topical

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•Bacterial Resistance•

- ↑↑ Resistance to oral & topical antibiotics in about 61% of acne ptn to → Erythromycin, → Clindamycin
  Less to → tetracycline, → Doxycycline
- Strategies for Limiting antibiotic Resistance to P.acne and other Bacteria :-

[1] Combine topical Retinoid + Antimicrobial :-
Result in: → ↑ speed of Response, → Greater clearing, → Enhanced efficacy against comedones

[2] if the addition of antibiotic is Required

- Limit the use of antibiotics to short periods and discontinue when there is No further improvement or the improvement is only slight.
  - oral antibiotics → Ideally used for 3 months But 6-8 weeks into ttt → might be one appropriate time point at which to asses response to antibiotics
- Avoid use of antibiotics for maintinance Therapy
- Co-prescribe a BPO-containing product or use as wash out:
  - BPO → Reduce the likehood of antibiotic Resistant P.acnes emerging + Rapidly Reduces the number of senstive and resistant strains of P.acnes at the site of application.
  - Use BPO either Concomitantly or pulsed as an anti-Resistant agent.
  - Use BPO for 5-7 days Between Antibiotic Courses.
- Oral and topical Antibiotics should Not used as monotherapy
- Concurrent use of oral + topical antibiotics → should Avoided particularly if Chemically diffrent: 1. ↑ risk of Bacterial Resistance 2. No synergestic action
- Don't Switch Antibiotics without adequate justification;
- Use topical Retinoids for maintenance Therape & BPO added for antimicrobial effect if needed

1 Topical :-

- prescribed for: mild acne & appropiate Oral therapy → for moderate acne

1 Benzoyl peroxide 5%

- Bacteriostatic (D.t liberation of free O_2)
- has peeling effect + Comedolytic
- Disadvantage: slight irritation
  Bleaching of clothes

2 Topical Retinoids:

⊛ Tretinoin ⊛

- Retin-A 0.025%, - 0.05%, 0.1%
- Cream or gel
- effective Comedolytic agent
- effective as: single agent therapy in ptn & non inflammatory comedones
- Once daily applied
- Clinical improvement after 6 weeks
- Max improvement : 3-4 months
- Long lasting remission → maintained with Continued application of tretinoin on an infrequent Basis.

- Topical Retinoids → should be first line agents in acne maintenance Therapy

- Mechanism of action:
  - within the cell cytoplasm → Retinoic acid (RA) Binds to a Cellular RA-binding protien (CRABP) → which transports RA to the nucleus.
  - in the nucleus → RA Binds to specific nuclear Receptors
  - RAR activated By RA Binds to DNA → affecting different gene expression.
- Therapeutic effect of tretinoin:
  - ↓↓ Cohesiveness of abnormal Follicular epithelium
  - Alters microclimate of microComedo
  - Resolves mature Comedones
  - prevent new lesions
  - Enhances penetration of other Drugs
- Side effects:
  1- irritation: transient. minimized By starting & appropiate Dose + gradually ↑ Concentration
  2- photo-irritation:

- Sunscreens: used in Conjunction e- application of tRetinoin By night Beause of its photo irritant effect

⭐ Adapalene 0.1% ⭐

(Differin gel)

- Stable naphthoic acid è potent Retinoid pharmacology → Controlling cell proliferation and Differentiation
- has significant anti-inflammatory action
- has less irritancy when it is Compared with topical tretinoin
- Mechanism of action:
- It Desn't Bind to Cellular retinoic acid-binding proteins (CRABP)
- It Binds to nuclear retinoic Receptors (RAR)
- Specially RAR-B > RAR-γ
- applied once daily
- compared to: topical tretinoin gel 0.025%
- more effective Better tolerated in tt of Acne.

⭐ Tazarotene ⭐

- synthetic acetylenic retinoid → once applied it is converted to its active metabolite
- Tazarotenic acid → selectivly Binds RARβ But Not RXR
- in the tt of acne → Result in regulation of follicular Corneocyte cohesion and normalization of keratinization

⭐ Combination retinoid-based Therapy is first-line Therapy for acne:-

1- Combination of Topical retinoid + antimicrobial agent (the preferred approach for almost all ptns è acne)

2- This Combination attacks 3-4 pathogenic factors of acne:
- abnormal desquamation
- P.acne colonization
- inflammation

Retinoids are:- anticomedogenic. Comedolytic have some anti-inflammatory effects

BPO:- is:- antimicrobial è some keratolytic effect and antibiotics have anti-inflammatory + anti-microbial effect

3- Fixed-Dose comination è topical Retinoids and antimicrobia → improved ptn convenience that may translate to improve adherence.

(*) Topical Retinoids should be first-line agents in acne maintenance therapy?

1- Studies show that topical Retinoid can maintain improvement achieved è Combination therapy

2- Topical Retinoid are Logical choice For maintenance therapy:
↳ Target microcomedo and prevent formation of Both comedones and inflammatory lesions
↳ Don't Create Selective pressure on Bacteria
↳ No known additional safety issues è Long term use

3- These Recomendations for pt è mild to moderate Severly acne

4- diffrent approach for pt è Severe.

5- Long term use of Antibiotics → avoided Should be avoided

3 Topical antibiotics:

- e.g: Clindamycin (Dalacin-T)
  Erythromycin (Aknemycin 2%.)
- the use of topical antibiotics: may encourage the development of resistant organism Becuse there will always be a zone adjacent to the area of application where the concentration of the antibiotic is subtheraputic → may facilitate the development of antibiotic-Resistant strains of p. acnes.
- Erythromycin 4% + Zn acetate 1.2%. (Acnebiotic, Zineryl) → inhibit the Development of bacterial Resistance. To topical antibiotics D.t Zn acetate 1.2%.

4 Sulphur ppt 2% in Calamine lotion

5 Steroids topically: For short period for inflammatory lesions

6 Azelaic Acid 20% (Skinoren)

- naturally occuring saturated dicarboxylic acid
- Contain 9 Carbon atoms

- it is dervied from pityrosporum ovale
- Azelaic acid has anti-acne action through: ① normalization of the disturbed follicular Keratinization
② strong antimicrobial action
③ Anti-inflammatory effects By ↓↓ the relase of reactive oxygen species from neutrophils
- it has No effect on Sebaceas gland :-
- AA 20% is also effective in hyperpigmented Disorder e.g: melasma, lentigo maligna in arresting malignant melanoma progression
- The major advantages of AA 20% "Skinoren" :- in the treatment of acne vulgaris :
↳ its Reduced irritancy Compared è Benzoyl peroxide and tretinoin
↳ its Doesn't Bleach clothes or bed-linen Common complaint against Benzoyl peroxide.
↳ it doesn't produce Resistance in p. acne
- Indications for the use of AA 20% in acne :
* - as Single therapy :
1- in pts è mild to mild-moderate acne
2- who have predominantly Non-inflammed or inflamed lesions
3 - as maintinance therapy after oral therapy
* - As Combined therapy :
• Diane
• Oral antibiotics (Tetracycline, Erythromycin)

⑦ Topical Dapsone :

- Dapson gel 5%. (ACZone) →
↳ effective, safe, well-tolerated ttt for AV
↳ Anti-inflammatory propoities →
è Long use in ttt of- inflammatory dermatoses
↳ ch.ch By: Neutrophilic inflammation.

2 Systemic

1 Antibiotics:

a) Tetracyclines:

↳ Tetracycline (1gm daily)
- Better in empty stomach
- Contraindicated ⊘ pregnancy Hepatic, Renal impairment

↳ Doxycycline: (Vibramycin)
100 mg/daily

↳ Minocycline: (Minocin)
100 mg/daily

↳ Side effects:
- Blue-Black pigmentation
- metallic taste
- Hypersenstivity Reactions
- Serum sickness-like Reaction
  - occur within 3 mnths of ttt
    - ↳ Fever
    - ↳ malaise
    - ↳ arthralgia
- minocycline induce SLE and hepatitis

b) Macrolides:

↳ Erythromycin
(1gm daily)
specially in women who might become pregnant

↳ Azithromycin:
- (250 mg/3 times/week)
Dute Long half life of 68hr

↳ Clindamycin:
(Dalacine C)
150 mg/3 times/daily
- Risk of colitis

↳ Trimethoprim-Sulfamethoxazole
(Septrin)
400-600 mg/day

* Mechanism of Action of Antibiotics

- Inhibition of P. acnes → ↓ lipases and
- ↓ Chemotactic substances
- ↓ Complement pathway
- ↓ Neutrophil migration

* Sub-antimicrobial doses of Doxycycline: 20 mg/twice daily

has: antinflammatory (non-antimicrobial) propoties
- its effective in Acne ttt.

* Tetracyclines: Non-antibiotic properties and their clinical implications:

Therapeutic effect include:
- Rosacea
- Bullous dermatosis
- Neutrophilic Diseases.
- Pyodema gangrenosum
- Sarcoidosis
- aortic aneurysm
- Cancer metastasis
- periodontitis

Dermatologic	• Acne. • Rosacea. • Bullous dermatoses. • Sarcoidosis. • Kaposi's sarcoma. • Pyoderma gangrenosum. • Hidradenitis suppurativa. • Sweet's syndrome. • α1-antitrypsin deficiency panniculitis. • Pityriasis lichenoides chronica.
Non-dermatologic	• Rheumatoid arthritis. • Scleroderma. • Cancer. • Cardiovascular diseases: Abdominal aortic aneurysm, acute myocardial infarction. • Periodontitis.

Mechanisms of action of tetracycline & tetracycline derivatives in the treatment of skin disease

Tetracycline	Low compliance, GI upset.
Erythromycin	GI upset.
Minocycline	Vestibular involvement, th
Doxycycline	Photosensitivity, GI upset.
Trimethoprim-sulfamethoxazole	Bone marrow suppression

2 Hormones

* in ptn ē Severe ttt-Resistant acne
* who are Not candidate for Isotretinoin
* Hormonal influence :-
  - → adult-onset
  - → chronic inflammatory acne
  - → premenstrual flare
  - → Distribution of Lower face, Jaw line & chin
  - → excessive facial oilness
  - → Coexistent Hirsutism
  - → male pattern alopecia
* three 3 choices :

• **Estrogens**: suppress ovarian Androgen
- most Formula : Combine estrogen ē progestin → to minimize the Risk of Endometrial Cancer → occure ē unopposed estrogens.
- progestin have intrinsic androgenic activity
- Oral contraceptive formulations :- 2nd generation + Low androgenic progestin

• **Corticosteroids**: supress adrenal androgen
- Short Courses of systemic Steroids (D.t anti-inflammatory effect)
  - in sever and cystic acne
  - acne Conglobata.
- Low Dose glucocorticoids → have anti-inflammatory and androgen inhibiting effects

3 • Anti-androgen :

→ [I] Cyproterone acetate (CA)

- synthetic non-estrogenic Compounds → Interfere with Binding of androgen with its Target organs (Sebaceous glands - hair bulbs - gonads)
- Indications :
  - → female ē Seborrhea
  - → AV
  - → Hirsutism
  - → Androgenic alopecia
- Side effects :
  - → inhibition of ovulation
  - → Spermatogenesis
  - → weight gain
  - → male featus :- Hypospadias inhibit scrotal develop.

- Contraindications: male
  female pregnant

- Dose: as OCPs
  100 mg daily → From 5th day of menstruation to 14th Day
  + 50 µg ethinyl estradiol
  From 5 till 25 of each cycle
  - For 3 - 12 months

Diane:	Diane-35	AndroCur
2 mg CA + 50 µg EE	2 mg CA + 35 µg EE	10 + 50 = 10, 50 mg CA

↳ [2] Spironolactone:
50 - to - 200 mg/daily

↳ [3] Flutamide, Cimetidine
Ketoconazole

[4] Oral Retinoids

Indications:

1- Sever acne Rosacea
2- Pyoderma Faciale
3- Severe acne: < Nodulocystic acne / sever inflammatory acne & Scarring
4- moderate acne: Not Responding to - or relapsed after conventional combined oral and Topical antibiotics For 6 months
5- Sever Psychological Distress.
6- Gram -ve folliculitis
7- Acne fulminans (preceded By: oral steroid therapy)
8- Hidradenitis Suppurativa
9- Acne Conglobata

Dose:

- 0.5 - 1 mg/kg For 4 - 5 months
- Cumulative dose: 120 - 150 mg/kg
- when to give Max Dose (1 mg/kg/d):
  ↳ if we don't have too much time e.g: few months For marriage.
  ↳ as Isotretinoin Must stopped At least one month before marriage → Fear of teratogenicity
- High Dose → under strict supervision.
  1.5 mg/kg or greater for 5-6 months (Cumulative dose of 290 mg/kg) → Reported Safe and effective For Sever Nodulocystic Acne.
- who use Dose of 220 mg/kg → significant ↓↓ Risk of relapse compare to Dose < 220 mg/kg

- Both:

Intermittent Dose [0.5-0.7 mg/kg/day] for one week of every 4 week

+ Continuous Low-Dose [0.25-0.4 mg/kg/day] for 24 week

↓

were Reported to be well tolerated and effective as classical Regimens in Tt of moderate acne vulgaris

- who should tte Dose < 0.5

- Gram-ve folliculitis
- Severe acne Rosacea
- Adult-onset acne
- Sebaceous Dermatitis
- Hidradenitis suppurativa
- Fordyce Disease.

Mechanism of Action:

1. Sebum suppression
2. Normalization of follicular epithelial desquamation
3. P. acnes Reduction
4. Anti-inflammatory:
   - DownRegulates TLR
   - Block Relase of proinflammatory cytokines
   - Block cellular inflammation
   - inhibit leukocyte migration
   - inhibit AP1 pathway

Side effects:

① Teratogenicity:

→ Avoid use in female in Child-bearing period except c` Concurrent use of Contraceptives.
→ 2 contraceptive methods should Be used. During and For 1 month after Therapy.
→ -ve pregnancy urine, Blood test → 1wk prior Tt.

② Acne flare:

- Early in the course of treatment in 6-30% of ptns
- in the 1st month of therapy and Regress in 2 weeks
- Risk Factors:

presence of Macro-Comedones and Nodules

- Oral prednisolone: 0.5 mg - 1.0 mg/kg/day for 2-3 weeks or till subside of flare

③ Cheilitis - Conjunctivitis - Nasal Dryness - Dermatitis

④ ↑↑ in Liver function tests: Return to normal after Tt stopped

⑤ Depression:

⑥ Inflammatory Bowel Disease: IBD

Ⓐ Isotretinoin Monitoring :-

- CBC • liver function test
- Serum lipids → Before starting and while on therapy
- ptns è strong family History of Coronary artery Disease OR Hyperlipidemia → given ttt è close follow up of
  - ↳ serum triglycorides + Cholesterol (Recommended)
- Monitoring Skeletal toxicity During a single course of therapy Not → indicated.

Ⓐ When to Stop Isotretinoin :-

① elevated liver enzymes

- Transaminase elevation to Greater Than 3 times the upper limit of normal → stop therapy

② if fasting triglycorides Reach 800 mg/dL :-

- less severe → treated è dose Reduction
- withdrawing therapy until normal-ization of serum lipids occur

④ ptn experiancing
- → abdominal pain
- → Rectal Bleeding
- → Sever Diarrhea (IBD)

Discontinue Therapy

Ⓐ AAD updated its position of Isotretinoin noting in a pair :-

- Correlation Between Isotretinoin use and depression/anxiety Symptoms → has been suggested But evidence-based Causal relationship Not established
- othe study give evidence that treatment of acne with Isotretinoin accompanied By :
  - ↳ improvement of Both depressive, anxiety & ↳ improve quality of life of ptne acne.
- The association concludes that the prescription of Isotretinoin for Sever nodular acne → Continuous to be appropiate as Long as prescribing physicians are aware of the issues related to Isotretinoin Use including :
  - → IBD → psychiatric disturbance
  - physicans should monitor there ptns for any IBD and depressive symptoms
- iPLEDGE program : FDA approved managment program for prescribing Isotretinoin : Online internet Sharing - use - presenting without physician Supervision

Common & some uncommon side effects of isotretinoin and their management

Side effect	Mild	Moderate	Severe
Cheilitis Facial dermatitis Discoid dermatitis Xeroderma	Lubricant	Intermediate steroid ointment	Potent steroid ointment combined with antiseptic & oral antibiotic
Nasal dryness & soreness	Lubricant	Nasal mupirocin	Nasal mupirocin + oral antibiotic
Blepharoconjunctivitis	Lubricant	Mild steroid/antibiotic combination	Antibiotic eye ointment + oral antibiotics
Arthralgia & myalgia	Nil	Paracetamol, aspirin, non-steroidal	
Headache	Nil	Paracetamol, dose reduction	Consider BIH*, stop therapy
Pyogenic granuloma	Nil	Potent steroid ointment + cautery & curettage	

Note: If in doubt, reduce the dose of isotretinoin. *BIH: Benign Intracranial Hypertension.*

5 other Oral therapy

Metformin

-use metformin for specific cases of acne as: acne result from Hormonal imbalance Caused By: abnormal Ovarian conditions: PCOS

Oral Zinc

Zinc gluconate (200 mg/day)

NSAIDS

Ibuprofen - 5-lipoxygenase inhibitor → ↓ inflamed lesion

Clofazimine

200 mg/3 times/day week → improve acne fulminans

Dapsone

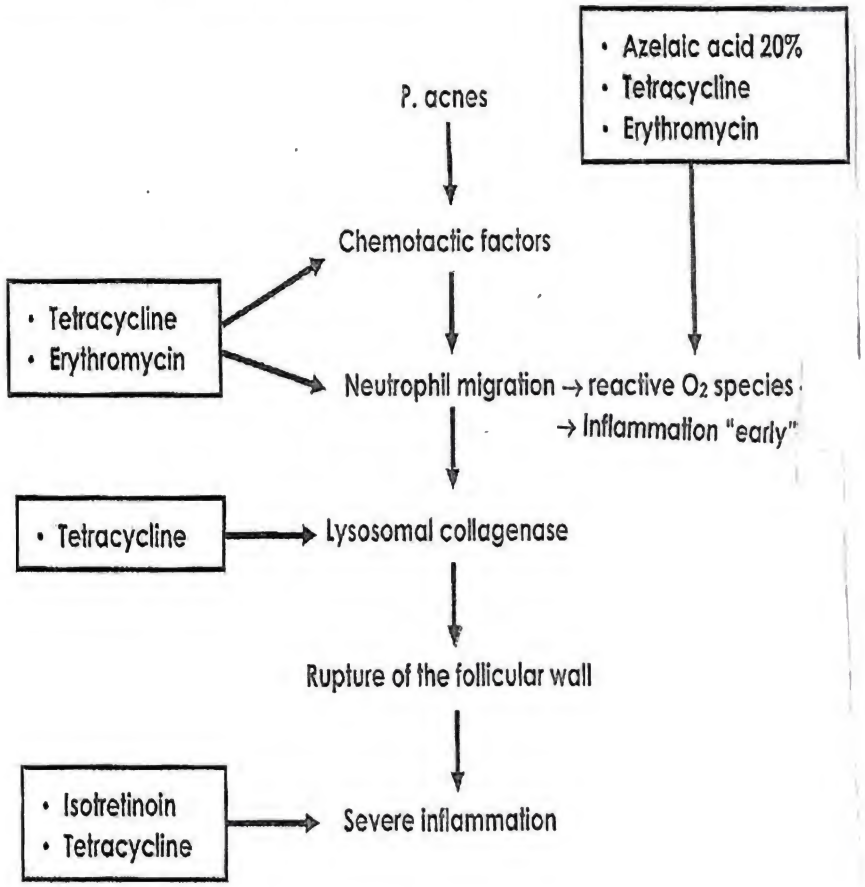
100-300 mg/day for 6 months G6PD Level Must checked Before ttt

Oral Vitamin A

Oral Predinsone 0.5-1 mg/kg/day

-Sever inflammatoy acne vulgaris
-Acne Fulminant - Pyoderma Faciale

Anti-inflammatory effects of acne therapy



3 other Lines of Tt

1 Physical

* Acne treatment with Light

1- Ultraviolet light is Not theraputic for AV
2- Blue light → has anti-inflammatory effect
3- Bright sunlight throw window glass → may improve acne in some ptns
4- Photodynamic Therapy using topical porphyrin pre cursor → Acne Respond well to i
5- more data needed for Laser & light

* Extraction of Comedones :-

- By Comedo extractor: Stages:
  - Softening the Comedones
  - Cleaning and Sterilizing the skin
  - Expressing the content of the Comedones
  - Cleansing the affected area.
- By Light Cautery after EMLA application

* Intralesional Coiticosteroid injection ↓ For Nodulocystic Lesion
* Cryotherapy
* Cosmetic Camouflage

2) treatment of acne scar

2) **Treatment of acne scars***

Punch excision (deep bases)	Combined therapy	**Shallow** ≤ 3 mm diameter – laser skin resurfacing	Intralesional corticosteroids	Intralesional steroids
Elevation & grafting	Micrograft & subcision +	>3 mm diameter – laser skin resurfacing + punch elevation	Intralesional 5-FU Intralesional bleomycin	Intralesional 5-FU Vascular laser
Laser resurfacing / dermabrasion (many scars close together)	± Filler	**Deep** ≤ 3 mm diameter – punch excision	Compression	Intralesional bleomycin Compression
Spot TCA peel (Fig. 42)	Resurfacing microderm-abrasion Deep – spot TCA peel **(CROSS technique)**	>3 mm diameter – Punch excision or punch elevation Fractional laser thermolysis (deep or shallow) Dermabrasion CO_2 laser resurfacing	Imiquimod after intralesional excision Cryotherapy Pulsed-dye laser Excision + electrotherapy	Imiquimod after intralesional excision

Early, appropriate treatment is the best to minimize the potential for acne scars*

- Scarring is often the primary concern of a patient with acne
- The treatment approach is usually determined by the scar characteristics and may involve resurfacing, surgical revision, and use of dermal fillers; in many cases, topical retinoids are a useful adjunct to procedures in management of scarring
- Two key modifiable factors are linked to acne scars: A time delay between onset of acne and effective treatment and the extent/duration of inflammation
- Early appropriate treatment that is continued for as long as necessary is the best way to prevent acne scarring
- The progression of scarring despite aggressive traditional treatment is a primary rationale for use of oral isotretinoin.

a Dermaroller

(Microneedling - Collagen induction)

- office procedure after application of Local anesthetic cream
- it's a: Simple - hand-held instrument Consisting of a handle with cylinder studded all around with fine - stainless steel needles 0.5 – 2mm
- This needle - studded cylinder is Rolled on the skin in multiple directions to achieve a therapatic Benefit
- These needles Cause: small pinpoint injuries on treated skin → heal within 2-3 days with NO post tt sequelae.
- treatment è dermaroller is performed at 4 to 8 weeks intervals
- Advantages: over laser resurfacing
  - ↳ NO epidermal injury
  - ↳ minimal Down time associated with the procedure
  - ↳ Far cheaper than laser
  - ↳ performed in office setting and doesn't need any extensive training
- Can used alone or Followed By: peel.

b CROSS technique

- Chemical Reconstruction Of Skin Scar.
- Technique using high Strength TCA
- (up to 100%)
- Focally on atrophic scar acne to induce Collagenization and Cosmetic improvement

c platelet rich plasma

- For atrophic acne scars
- The physiological effect of PRP Based on the relase of:-

1- ↳ Growth factors from platelat granules including → PDGF, IGF ← VEGF, EGF

2- ↳ proteins that influence wound healing, derived from α-granules of activated platelats includes:
- ↳ Osteocalcin (Oc)
- ↳ Osteonectin (On)
- ↳ Vitronectin (Vn)
- ↳ Fibronectin (Fn)

- PRP → used as adjuvant Therapy for Laser
- treatment of atrophic acne skars -

3↳ PRP + ablative O2 fractional resurfacing: or erbium fractional laser therapy:.
effective - safe for ttt acne scars. with minimal side effects
- Simultaneously enhance the Recovery of Laser Damaged - skin.

4- ↳ PRP applied:
topical or intradermal after fractional ablative Carbon Dioxide Laser ttt.
topical → more tolerated

d CO_2 Laser resurfacing

- for modrate to severe atrophic acne scars
- Safely improved By ablative fractional CO_2 laser resurfacing
- FAST: technique "Focal Acne Scar treatmat" using fractional CO_2 laser resurfacing in treating The acne scars only and leaving Normal skin untreated.

3 General measures

- Assurance - Avoid stress
- Stop squeezing lesions
- Frequent washing face e~ antiseptic soap
- avoid heavy cosmetic prep.
- Cosmeceutical approach is important to acne ptns.

Skin Care for Oily Skin & acne

- Daily cleansing e:- foaming gel cleansers
  e.g: Sebium foaming gel
  Sebium H_2O
  Sebium Soap
- The effect is beneficial of antibacterial soaps containing material as: triclosan remains Controversal
- for photoprotection:- use fluid sunscreen (Photoderm)

with Isotretinoin treatment

- The oiliness of Skin → Reduces
- Skin Become Dry SO changing to Moist
- urizing protocol Must
  - emollients (Sensibio light . Atoderm)
  - emollients Con Light & exture & Soothing effect
  - for photoprotection Sunscreen Creams (Photoderm Cream)

Anti-Acne Agents

Anti-acne agents	Sebum excretory rate	Microbial population	Inflammation	Follicular keratinization	Side effects
Tetracycline (S)	-	++	+	-	Antibiotic resistance
Isotretinoin (S)	+++	+	++	++	Teratogenic + muco-cutaneous effects
Cyproterone acetate (S)	++	-	-	-	Teratogenic + sperm abnormalities
Benzoyl peroxide(T)	-	+++	+	+	Irritation
Erythromycin (T)	-	++	-	-	Resistance
Clindamycin (T)	-	++	-	-	Resistance
Tretinoin (T)	-	+	-	++	Irritation
Azelaic acid (T)	-	++	+	++	-------

• Acneiform Eruptions •

• D.F :- papules - pustules resembling AV But differ in :- Not confined to the usual sites of AV • sudden onset • in ptn passing acne age • resolve slowly with withdrawal of the cause.

• Types:

[1] Epidermal growth Factor receptor (EGF-R) inhibitor-induced Eruption:

- Drugs used for Tt of solid Tumors
- EGF-R → strongly expressed in Keratinocytes and in cells of eccrine and apocrine glands
- inhibition of EGF-R → disturbs the nomal diffrentiation and morphogenesis of hair follicles
- excessive follicular Hyperkeratosis
  follicular plugging

[2] Tropical Acne : tropics - Hot - humid.

- Nodular and Cystic lesions leaving scars on : Back - shoulder - arm
  Sparing Face

[3] Acne aestivalis :

- acne Start :- in spring → progress in summer
  Resolve in : Fall.
- affect :- women 25-40 yr
- lesion : Erythematous Small papules
- Develop on the cheeks - Sides of Neck - upper arm
  - without pustules or Comedones
- Tt :- Retinoic acid

[4] Radiation Acne :

Comedo-like papules at site of previous expssure to therapeutic ionizing radiation

[5] Pseudo-acne : of transverse nasal crease.

- Horizontal anatomical demarcation line found in Lower third of the nose
- Milia - cyst - Comedones

[6] Idiopathic facial aseptic granuloma

- Chronic - painless - solitary nodule - cheeks of young children - Resolve spontenously after 11 month

[7] Childhood flexural Comedones :

Discrete - Double orifice Comedones in axilla

[8] Acne keloidalis nuchae

[9] Pseudofolliculitis Barbae

[10] Perioral Dermatitis
Periorofacial dematosis

[11] Acne inversa:
Hidradenitis Suppurativa

• Spectrum of acne and acne-related Dermatoses •

① Related to intrinsic Causes
- Acne vulgaris
- Perioral Dermatitis
- Acne Conglobata
- Hidradenitis suppurativa
- Pyoderma faciales

② Related to extrinsic Cause:
- acne excorée des jeunes filles
- acne Mechanica
- acne tropicalis
- Acne Aestivalis
- Favre-Racouchat's
- pomade acne
- Drug-induced acne
- Acne Cosmetica
- occupational Acne.

③ Childhood Acne: Neonatal acne, infantile acne

④ Acneform eruption: Rosacea, Acne keloidalis nuchae, Gram -ve Folliculitis, Steroid acne

• Causes of Comedones •

① Primary developmental defect of the follicle
- Nevus comedonicus
- nevoid Follicular Epidermolytic Hyperkeratosis

② Genetically Determined abnormality of Pilosebaceous function:
- Acne vulgaris
- familial comedones → autosomal Domint with mono-poly porous comedones

③ Disturbed follicular Keratinization
By:
- exogenous acneigenic agents
- Acne venenta
- Acne medicamentosa

④ injury to pilosebaceous follicles By ionizing Radiation

⑤ Connective tissue Abnormalities:- Necrobiosis Lipodica

Differential diagnosis of acne

Acne vulgaris (comedonal)

- ***Closed:***
  - Milia.
  - Osteoma cutis.
  - Sebaceous hyperplasia.
  - Syringomas.
  - Trichoepitheliomas*.
- ***Open:***
  - Contact acne.
  - Acne exacerbated by systemic corticosteroids & anabolic steroids.
  - Favre-Racouchot disease.
  - Nevus comedonicus.

Acne vulgaris (inflammatory)

- Rosacea.
- Perioral dermatitis.
- Folliculitis-culture-negative (normal flora), staphylococcal, gram-negative, eosinophilic, Pityrosporum, Demodex.
- Acne/acneiform eruptions due to topical or systemic corticosteroids**, anabolic steroids or other medications (e.g. lithium, EGFR inhibitors).
- Pseudofolliculitis barbae, acne keloidalis nuchae.
- Furuncle / carbuncle.
- Lupus miliaris disseminatus faciei.
- Neurotic excoriations / factitial.

Neonatal acne (neonatal cephalic pustulosis)

- Sebaceous hyperplasia.
- Milia.
- Miliaria rubra (especially pustular variant).
- Candidal infections.

Acne

	Acne vulgaris	Lupus miliaris disseminates faciei
CP	- Comedones, papules, pustules, nodules, cysts - Face, chest, shoulders, upper back - Post-inflammatory erythema & pigmentation - May heal with scarring - Seborrhea	- Discrete, reddish papules - Face mainly eyelid, cheeks, upper lip - Absent erythema & telangiectasia - Involutes spontaneously with pitted small scars
HP	1- Comedone → keratinous debris, micro-organism, hair, sebum 2- papules → lymphocytic perifollicular infiltrate 3- Rupture of follicle wall → escape of contents → aggregation of neutrophils → pustules & nodules	1- Large tubercle → epitheliod cells & giant cell 2- Central caseation necrosis 3- Peripheral inflammatory infiltrate
Pathogenesis	1- Increased sebum production 2- Ductal hypercornification 3- Proliferation of P.acne 4- Inflammation	1- No evidence support tubercle etiology 2- It may be related to rasacea
ttt	Anti-acne agents	Tetracycline, minocycline, isotretinoin

٣+

Acne

Neonatal acne	Infantile acne
- May be present at birth or develop during the 1st few months - More common in males - Mild & regress spontaneously by the age of 6 months - Not associated with significant scarring or increased incidence of acne later in life	- Begins between 3rd & 6th month - More common in males - Severe nodules & cysts & may persist to age of 5 years - Associated with significant scarring or increased incidence of acne later in life - Associated with vililizing tumors
Pathogenesis: - Species of malassezia - Response to topical ketoconazole - Sebum excretion: high level	- Intrinsic hormonal imbalance ↑ testosterone, LH, DHEA

أسأل كم الدعاء لي

Acne vulgaris	Acneiform eruption
- Comedone, papule, pustule, nodules, cyst - Face, chest, shoulders, upper back - Age: male: 16-19, females: 14-16 - Chronic inflammatory disorder - Acne variants: .... - ttt: anti-acne agent	- Papule, pustule - Not confined to the usual sites - Passing acne age - Sudden onset - Types: ... - Resolve slowly with withdrawal of the cause

(18)

Q Acne:

1- Pathogenesis of acne vulgaris.
2- Give an account on acne vulgaris
3- Give an account on Acne variants.
4- Pathogenesis, clinical types & therapeutic modalities in acne vulgaris.
5- Compare between acne conglobata & acne fulminans.
6- Compare between Acneform eruptions & acne vulgaris
7- Compare between neonatal acne & infantile acne
8- Management and Medical ttt of nodulocystic acne.
9- Acneform eruptions.

10- Preoperative considerations of laser ttt of acne scar
11- Compare: AV & drug induced acne
12- Compare: AV & lupus miliaris disseminated faciei
13- CP & management of rosacea
14- Eye manifestations of rosacea
15- Ecrine & apocrine sweat gland: distribution, histological shape, location, mechanism of secretion, diseases affecting them
16- Hyperhidrosis, causes, clinical variants & ttt

acne

1) acne varint ?

1. اهم واحدة acne fulminant clinically? Ttf?

2) classification of acne ?

عاوز يسمع inflammatory and non inflamtory

a. مش عاوز يسمع mild,mod.severe

3) Gram negative folliculitis

4) Isotretinoin cumulative dose مهم جدا

امتى ندى اقل من ٠.٥ مجم فى اليوم فى الروزسيشيا

5) Acne fulminans and conglobata ?

6) Why is hemorrhagic nodul in acne fulminans ? vascular

7) Systemic maniefest of acne fulminans ?

8) Lupus milliaris ?

9) Compare Lupus milliaris and acne ?

10) pAthogenesis of acne ?

11) syndrome associated with acne?

12) Emergency of acne ?

13) Type of comedo of acne conglobata ?

14) Reason and ttt of an fulminans and conglobata?

15) Low dose uses of isotretinoin?

16) اكتب روشتة لحب الشباب ؟ ده سؤال روتينى ف الشفوى

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